

Denosumab (XGEVA) and risk of osteonecrosis of the jaw: new contraindication and introduction of a patient reminder card to minimize the risk.

Dear Healthcare Professional,

Amgen Ltd, in agreement with the European Medicines Agency and Malta Medicines Authority, would like to inform you of a new contraindication in patients with unhealed lesions from dental or oral surgery, revised warnings and precautions and the introduction of a patient reminder card, to minimise the risk of osteonecrosis of the jaw (ONJ) during treatment with XGEVA.

Summary

- **XGEVA is now contra-indicated in patients with unhealed lesions from dental or oral surgery.**
- **A patient reminder card is introduced to increase patients' awareness for the risk of ONJ and the necessary precautions to minimize this risk.**
- **Patients treated with XGEVA should be given this patient reminder card with information on ONJ, as well as the package leaflet.**

Further information on the safety concern

ONJ is a common side effect in patients treated with XGEVA (may affect up to 1 in 10 people).

The product information is being updated to reflect the current knowledge on ONJ and to optimize risk minimisation.

Changes to the product information include the addition of a contraindication in patients with unhealed lesions from dental or oral surgery to ensure that treatment is not initiated when the patient is in this situation. A dental examination with preventive dentistry is recommended prior to treatment with XGEVA.

The management plan of any patients who develop ONJ should be set up in close collaboration between the treating physician and a dentist or oral surgeon with expertise in ONJ.

Why these changes are being introduced

The European Medicines Agency (EMA) recently undertook a review of the effectiveness of risk minimisation measures regarding the risk of osteonecrosis of the jaw (ONJ) with bisphosphonates and denosumab. This has resulted in a recommendation that reinforced safety messages be reflected in the product information (which contains the SmPC and package leaflet) for these products, as well as introduction of a patient reminder card, giving details of precautions to take to minimise the risk for ONJ.

The card will remind patients about important safety information that they need to be aware of before and during treatment with denosumab (XGEVA) injections for cancer-related conditions, including:

- to tell their doctor/nurse if they have any problems with their mouth or teeth to before starting treatment;
- to maintain good oral hygiene and receive routine dental check-ups during treatment;
- to inform their doctor and tell their dentist that they are being treated with denosumab (Xgeva) if they are under dental treatment or will undergo dental surgery
- to contact their doctor and dentist immediately if they experience any problems with their mouth or teeth such as loose teeth, pain or swelling, non-healing of sores or discharge

You will receive copies of the patient reminder card with this letter.

Further information on the product

XGEVA is indicated for:

- the prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumours.
- treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity

Call for reporting

▼ This medicine is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions to the Medicines Authority by post or e-mail: ADR reporting/ Sir Temi Zammit Building, Malta Life Sciences Park, San Gwann or on www.medicinesauthority.gov.mt/adrportal

Contact details

Should you have any questions or require additional information regarding the use of XGEVA please contact pharmacovigilance@cherubino.com.mt

Additional copies of the patient reminder card be requested by e-mail on pharmacovigilance@cherubino.com.mt or care@cherubino.com.mt or elaine@cherubino.com.mt

Sincerely

Luisa De'Piro O'Connell

Annex

Patient reminder card regarding osteonecrosis of the jaw

This reminder card contains important safety information that you need to be aware of before and during treatment with denosumab (XGEVA) injections for cancer-related conditions

Your doctor has recommended that you receive denosumab (XGEVA) injections to help prevent bone complications (e.g. fractures) caused by bone metastases, or bone cancers.

A side effect called osteonecrosis of the jaw (ONJ, bone damage in the jaw) has been reported commonly (may affect up to 1 in 10 people) in patients receiving denosumab (XGEVA) injections for cancer-related conditions. ONJ can also occur after stopping treatment.

It is important to try to prevent ONJ developing as it may be a painful condition that can be difficult to treat. In order to reduce the risk of developing ONJ, there are some precautions you should take:

Before starting treatment:

- Check with your doctor whether a dental examination is recommended before you start treatment with denosumab (XGEVA).
- Tell your doctor/nurse (health care professional) if you have any problems with your mouth or teeth.

Patients undergoing dental surgery (e.g. tooth extractions), who do not receive routine dental care or have gum disease, are smokers, who get different types of cancer treatments may have a higher risk of developing ONJ.

While being treated:

- You should maintain good oral hygiene and receive routine dental check-ups. If you wear dentures you should make sure these fit properly.
- If you are under dental treatment or will undergo dental surgery (e.g. tooth extractions), inform your doctor and tell your dentist that you are being treated with denosumab (XGEVA).
- Contact your doctor and dentist immediately if you experience any problems with your mouth or teeth such as loose teeth, pain or swelling, non-healing of sores or discharge, as these could be signs of ONJ.

Please read the package leaflet that comes with your medicine for further information.

